What is claimed is:

1. A polynucleotide comprising a non-naturally occurring HCV sequence that is capable of productive replication in a host cell, or is capable of being transcribed into a non-naturally occurring HCV sequence that is capable of productive replication in a host cell, wherein the HCV sequence comprises, from 5′ to 3′ on the positive-sense nucleic acid, a functional 5′ non-translated region (5' NTR); one or more protein coding regions, including at least one polyprotein coding region that is capable of replicating HCV RNA; and a functional HCV 3′ non-translated region (3' NTR).

2. The polynucleotide of claim 1, further comprising an adaptive mutation.

3. The polynucleotide of claim 2, having a transfection efficiency into mammalian cells of greater than 0.01%.

4. The polynucleotide of claim 2, wherein the transfection efficiency into mammalian cells is greater than 0.1%.

5. The polynucleotide of claim 2, wherein the transfection efficiency into mammalian cells is greater than 1%.

6. The polynucleotide of claim 2, wherein the transfection efficiency into mammalian cells is greater than 5%.

7. The polynucleotide of claim 2, wherein the polynucleotide is capable of replication in a non-hepatic cell.

8. The polynucleotide of claim 6, wherein the non-hepatic cell is a HeLa cell.

9. The polynucleotide of claim 2, wherein the HCV is impaired in its ability to cause disease, establish chronic infections, trigger autoimmune responses, and transform cells.

10. The polynucleotide of claim 2, wherein the polyprotein region comprises an NS5A gene that is not a wild-type NS5A gene.

11. The polynucleotide of claim 10, wherein the NS5A gene comprises a mutation.

12. The polynucleotide of claim 11, wherein the mutation is within 50 nucleotides of an ISDR or includes the ISDR.

13. The polynucleotide of claim 12, wherein the mutation is within 20 nt of the ISDR, or includes the ISDR.

14. The polynucleotide of claim 13, wherein the mutation encodes an amino acid sequence change selected from the group consisting of Ser (1179) to Ile, Arg (1164) to Gly, Ala(1174) to Ser, Ser(1172) to Cys, and Ser(1172) to Pro of SEQ ID NO:3.

15. The polynucleotide of claim 1, wherein the mutation comprises a deletion of at least a portion of the ISDR.

16. The polynucleotide of claim 15, wherein the mutation comprises a deletion of the entire ISDR.

17. The polynucleotide of claim 16, wherein the mutation comprises a deletion of nucleotides corresponding to nucleotides 5345 to 5485 of SEQ ID NO:6.

18. The polynucleotide of claim 1, wherein the polynucleotide comprises at least one IRES selected from the group consisting of a viral IRES, a cellular IRES, and an artificial IRES.

19. The polynucleotide of claim 18, wherein the HCV polyprotein coding region encodes all HCV structural and nonstructural proteins.

20. The polynucleotide of claim 19, further comprising a foreign gene operably linked to a first IRES and the HCV polyprotein coding region operably linked to a second IRES.

21. The polynucleotide of claim 18, wherein the polyprotein coding region is incapable of making infectious HCV particles.

22. The polynucleotide of claim 21, wherein the polyprotein coding region comprises a mutation and/or a deletion in the structural protein coding region.

23. The polynucleotide of claim 22, further comprising a foreign gene operably linked to a first IRES and the HCV polyprotein coding region operably linked to a second IRES.

24. The polynucleotide of claim 23, wherein the foreign gene is a gene encoding a selectable marker or a reporter gene.

25. The polynucleotide of claim 24, further comprising an adaptive mutation.

26. The polynucleotide of claim 25, having a transfection efficiency into mammalian cells of greater than 0.01%.

27. The polynucleotide of claim 26, wherein the transfection efficiency into mammalian cells is greater than 1%.

28. The polynucleotide of claim 26, wherein the transfection efficiency into mammalian cells is greater than 5%.

29. The polynucleotide of claim 26, wherein the transfection efficiency into mammalian cells is about 6%.

30. The polynucleotide of claim 25, wherein the polynucleotide is capable of replication in a non-hepatic cell.

31. The polynucleotide of claim 30, wherein the non-hepatic cell is a HeLa cell.

32. The polynucleotide of claim 25, wherein the HCV is impaired in its ability to cause disease, establish chronic infections, trigger autoimmune responses, and transform cells.

33. The polynucleotide of claim 25, wherein the polyprotein region comprises an NS5A gene that is not a wild-type NS5A gene.

34. The polynucleotide of claim 33, wherein the NS5A gene comprises a mutation.

35. The polynucleotide of claim 34, wherein the mutation is within 50 nucleotides of an ISDR or includes the ISDR.

36. The polynucleotide of claim 34, wherein the mutation is within 20 nt of the ISDR, or includes the ISDR.

37. The polynucleotide of claim 36, wherein the mutation encodes an amino acid sequence change selected from the group consisting of Ser (1179) to Ile, Arg (1164) to Gly, Ala(1174) to Ser, Ser(1172) to Cys, and Ser(1172) to Pro of SEQ ID NO:3.

38. The polynucleotide of claim 34, wherein the mutation comprises a deletion of at least a portion of the ISDR.

39. The polynucleotide of claim 38, wherein the mutation comprises a deletion of the entire ISDR.

40. The polynucleotide of claim 39, wherein the mutation comprises a deletion of nucleotides corresponding to nucleotides 5345 to 5485 of SEQ ID NO:6.

41. The polynucleotide of claim 24, wherein:

(a) the first IRES is an HCV IRES;

(b) the foreign gene is a *neo* gene; and

(c) the second IRES is a EMCV IRES.

42. The polynucleotide of claim 41, wherein the HCV sequence is a genotype 1 HCV sequence.

43. The polynucleotide of claim 42, wherein the HCV sequence is subtype 1b.

44. The polynucleotide of claim 41, comprising SEQ ID NO:5 or SEQ ID NO:6.

45. The polynucleotide of claim 41 further comprising an adaptive mutation.

46. The polynucleotide of claim 45, having a transfection efficiency into mammalian cells of greater than 0.01%.

47. The polynucleotide of claim 46, wherein the transfection efficiency into mammalian cells is greater than 1%.

48. The polynucleotide of claim 46, wherein the transfection efficiency into mammalian cells is greater than 5%.

49. The polynucleotide of claim 46, wherein the transfection efficiency into mammalian cells is about 6%.

50. The polynucleotide of claim 45, wherein the polynucleotide is capable of replication in a non-hepatic cell.

51. The polynucleotide of claim 50, wherein the non-hepatic cell is a HeLa cell.

52. The polynucleotide of claim 45, wherein the HCV is impaired in its ability to cause disease, establish chronic infections, trigger autoimmune responses, and transform cells.

53. The polynucleotide of claim 45, wherein the polyprotein region comprises an NS5A gene that is not a wild-type NS5A gene.

54. The polynucleotide of claim 53, wherein the NS5A gene comprises a mutation.

55. The polynucleotide of claim 54, wherein the mutation is within 50 nucleotides of an ISDR or includes the ISDR.

56. The polynucleotide of claim 54, wherein the mutation is within 20 nt of the ISDR, or includes the ISDR.

57. The polynucleotide of claim 56, wherein the mutation encodes an amino acid sequence change selected from the group consisting of Ser (1179) to Ile, Arg (1164) to Gly, Ala(1174) to Ser, Ser(1172) to Cys, and Ser(1172) to Pro of SEQ ID NO:3.

58. The polynucleotide of claim 54, wherein the mutation comprises a deletion of at least a portion of the ISDR.

59. The polynucleotide of claim 58, wherein the mutation comprises a deletion of the entire ISDR.

60. The polynucleotide of claim 59, wherein the mutation comprises a deletion of nucleotides corresponding to nucleotides 5345 to 5485 of SEQ ID NO:6.

61. The polynucleotide of claim 1, wherein the polynucleotide is double-stranded DNA.

62. A vector comprising the polynucleotide of claim 61 operably associated with a promoter.

63. The polynucleotide of claim 41 wherein the polynucleotide is double-stranded DNA.

64. A vector comprising the polynucleotide of claim 63 operably associated with a promoter.

65. The vector of claim 64, further comprising a mutation in the NS5A gene.

66. The vector of claim 65, wherein the mutation is selected from the group consisting of mutations encoding the amino acid changes Ser (1179) to Ile, Arg (1164) to Gly, Ala(1174) to Ser, Ser(1172) to Cys, and Ser(1172) to Pro of SEQ ID NO:3; and an in frame deletion of nucleotides encoding amino acids comprising at least a portion of the ISDR.

67. The vector of claim 66, wherein the mutation comprises a deletion of the entire ISDR.

68. The vector of claim 67, wherein the mutation comprises a deletion of nucleotides corresponding to nucleotides 5345 to 5485 of SEQ ID NO:6.

69. A cell comprising the vector of claim 62.

70. A host cell comprising the polynucleotide of claim 2, wherein the host cell is a mammalian cell.

71. The host cell of claim 70, wherein the polynucleotide comprises an adaptive mutation.

72. The host cell of claim 71 wherein the host cell is a human cell.

73. The host cell of claim 72 wherein the host cell is a liver cell.

74. The host cell of claim 72 wherein the host cell is a T-cell or a B-cell.

75. The host cell of claim 72 wherein the host cell is a HeLa cell.

76. A method for identifying a cell line that is permissive for infection with HCV, comprising contacting a cell in tissue culture with an infectious amount of the polynucleotide of claim 1, and detecting replication of HCV in cells of the cell line.

77. A method for producing a cell line comprising replicating HCV, the method comprising

(a) transcribing the vector of claim 62 to synthesize HCV RNA;

(b) transfecting a cell with the HCV RNA of step (a); and

(c) culturing the cell.

78. A vaccine comprising the polynucleotide of claim 1 in a pharmaceutically acceptable carrier.

79. The vaccine of claim 78, wherein the polynucleotide further comprises an adaptive mutation.

80. The vaccine of claim 79, wherein the adaptive mutation comprises a deletion of nucleotides corresponding to nucleotides 5345 to 5485 of SEQ ID NO:6.

81. The vaccine of claim 80, wherein the HCV is impaired in its ability to cause disease, establish chronic infections, trigger autoimmune responses, and transform cells.

82. A method of inducing immunoprotection to HCV in a primate, comprising administering to the primate the vaccine of claim 78.

83. A method of inducing immunoprotection to HCV in a primate, comprising administering to the primate the vaccine of claim 81.

84. A method of testing a compound for inhibiting HCV replication, comprising

(a) treating the host cell of claim 70 with the compound;

(b) evaluating the treated host cell for reduced HCV replication, wherein reduced HCV replication indicates the ability of the compound to inhibit HCV replication.

85. A method of testing a compound for inhibiting HCV infection comprising treating a host cell with the compound before, during or after infecting or transfecting the host cell with the polynucleotide of claim 1.